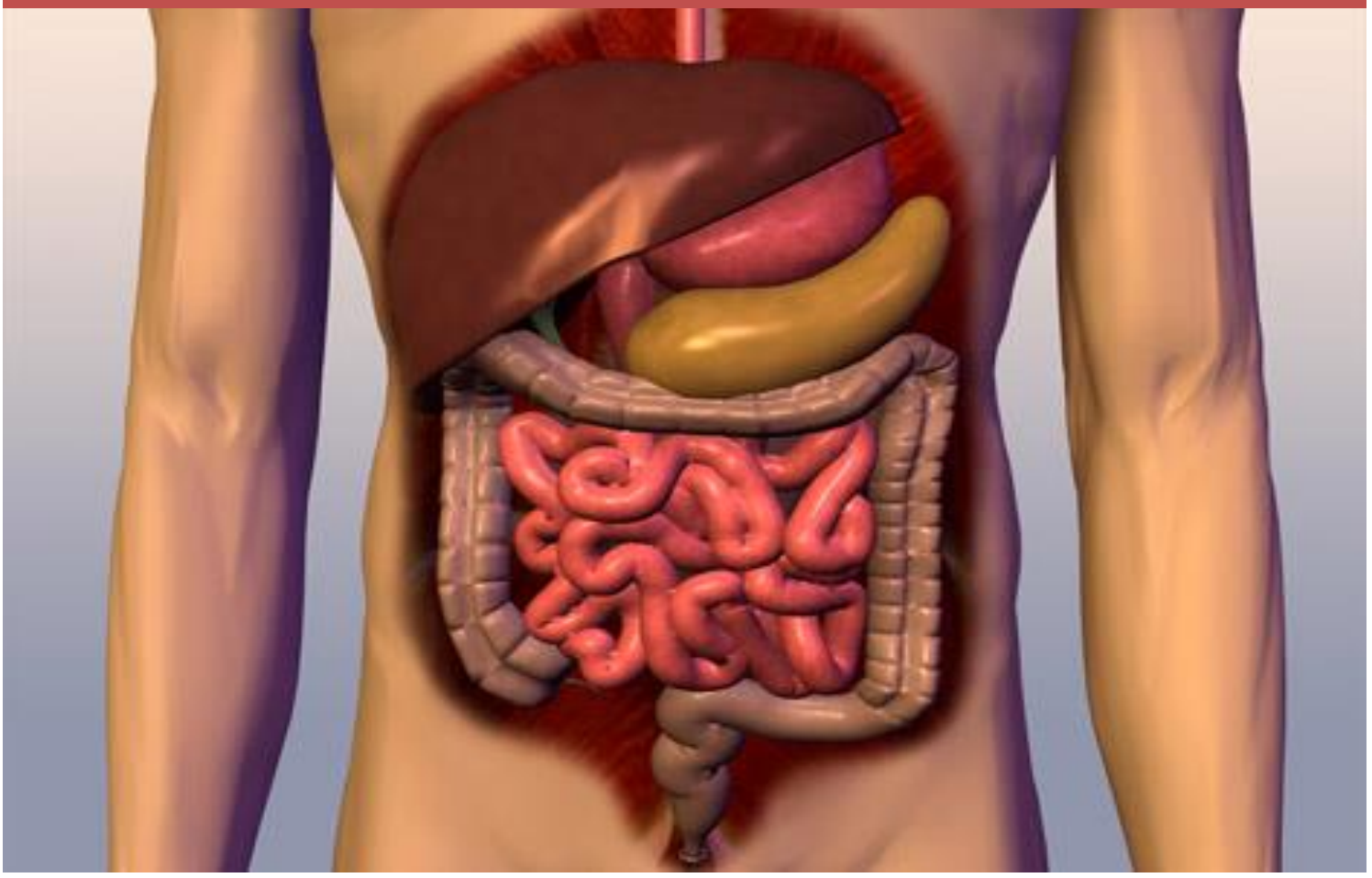

Lecture three

Malabsorption

432 ***Pathology*** *Team*

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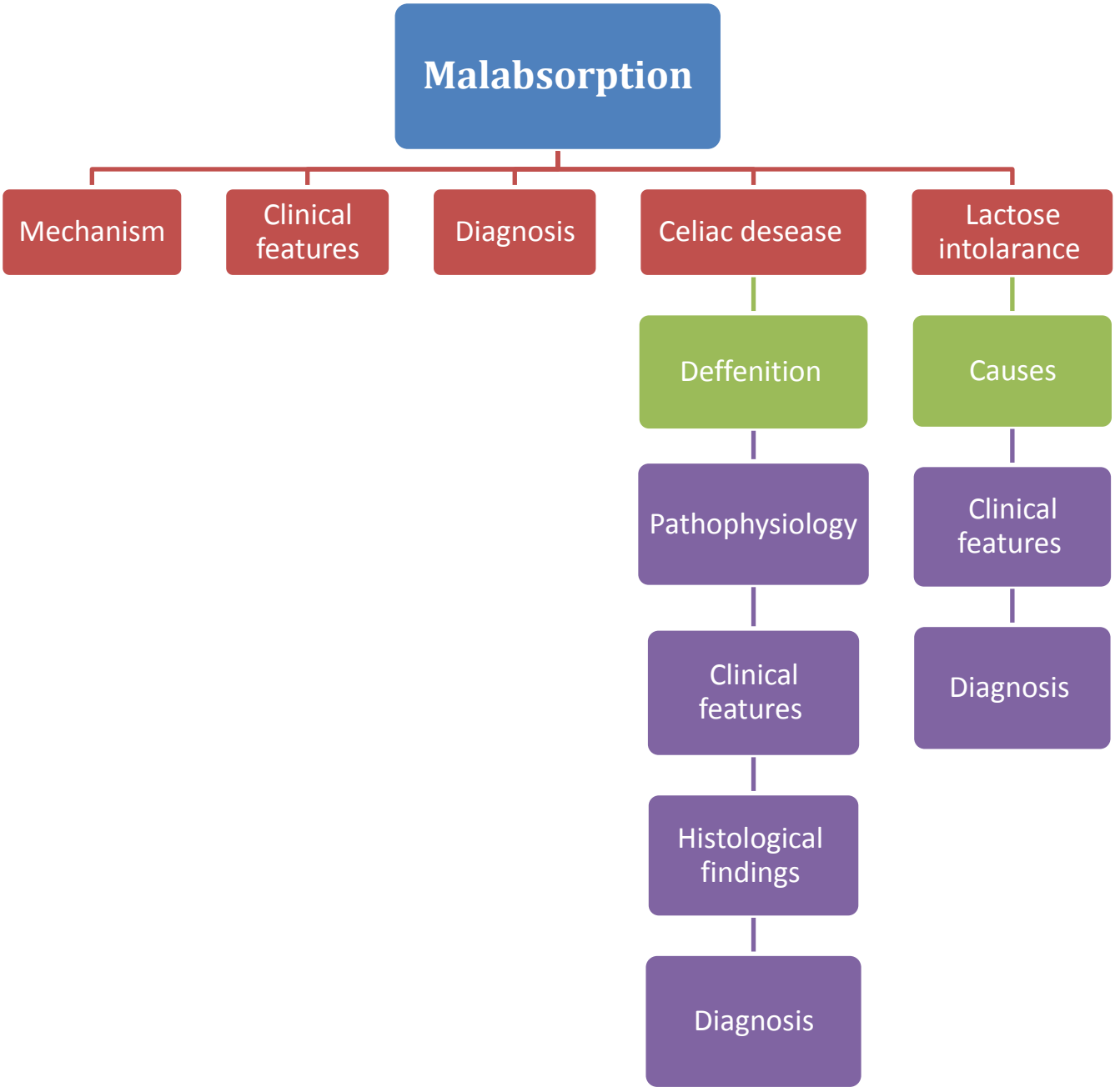
Reviewed By: Fahad *Alturki*

GIT Block

Color Index: female notes are in purple. Male notes are in Blue. Red is important. Orange is explanation.

Malabsorption

Mind Map:



Malabsorption syndrome

Definitions:

Malabsorption is the inability of the intestine to absorb nutrients adequately into the bloodstream; Impairment can be of single or multiple nutrients depending on the abnormality. (Example: the abnormality is in the bile system ➔there will only be a problem in the absorption of fat, and if it was in the small intestine ➔ all nutrients can't be absorbed)

The main purpose of the gastrointestinal tract is to digests and absorbs nutrients (fat, carbohydrate, and protein), micronutrients (vitamins and trace minerals), water, and electrolytes.

Mechanisms and Causes of Malabsorption Syndrome: (Have many causes)

1. Inadequate digestion:

(Postgastrectomy, Deficiency of pancreatic lipase, chronic pancreatitis, Cystic fibrosis, pancreatic resection, and Zollinger-Ellison syndrome).

2. Deficient bile salt:

(Obstructive jaundice, Bacterial overgrowth, Stasis in blind loops, diverticula, Fistulas, Hypomotility states (diabetes), Terminal ileal resection, Crohns' disease, and Precipitation of bile salts (neomycin)).

3. Primary mucosal abnormalities (the most important):

(Celiac disease, Tropical sprue, Whipple's disease, Amyloidosis, Radiation enteritis, Abetalipoproteinemia, and Giardiasis).

4. Inadequate small intestine

(Intestinal resection, Crohn's disease, Mesenteric vascular disease with infarction, and Jejunoileal bypass).

5. Lymphatic obstruction

(Intestinal lymphangiectasia, malignant lymphoma, Macroglobulinemia)

The Doctor said: "You may be asked about a disease that can cause malabsorption in the MCQs. So, you should go through all the names briefly.

NOTE:

Zollinger-Ellison syndrome: excessive production of (gastric secretions) acid interfere with the normal function of pancreatic enzymes (only work in alkaline media) interfere with food digestion.

Whipple's disease: is a rare condition that prevents the small intestines from properly absorbing nutrients. Whipple's disease is caused by infection with a bacterium called "Tropheryma whippelii".

Malignant lymphoma: is a malignant neoplasm which interferes with the absorption of food due to lymphatic obstruction leading to malabsorption.

Pathophysiology: (basic mechanisms)

1-Inadequate digestion

- **Stomach:** Postgastrectomy.
- **Pancreas:** Deficiency of pancreatic lipase, chronic pancreatitis, Cystic fibrosis, pancreatic resection.
- **Bile:** Terminal ileal resection, Obstructive jaundice.

2-Small intestine abnormalities

- **Mucosa:** Celiac disease, Tropical sprue, Whipple's disease, (caused by *Tropheryma whipplei)*, Giardiasis.
- **Inadequate small intestine**: Intestinal resection - Crohn's disease.
- **Lymphatic obstruction**: Intestinal lymphangiectasia - Malignant lymphoma.

(NOTE: our main focus is going to be on the "mucosa", the rest will be further discussed in upcoming lectures)

Clinical features:

1- Abnormal stools

- There is increased fecal excretion of fat (steatorrhea).
- Characteristic of stool: Stools become soft, yellow, malodorous (bad smell), greasy and floated at the top of the water in the toilet.

Quantitative stool for fat:
(1) Best screening test.
(2) 72-hour collection of stool.
(3) Positive test > 7 g of fat/24 hours.

2- Failure to thrive or poor growth in most but not all cases (Weight loss despite increased oral intake of nutrients). Especially in children.

3- Specific nutrient deficiencies, either singly or in combination.

Clinical features (that depend on the deficient nutrient):

- **Protein:** ⟶ swelling or edema – muscle wasting.
- **Vitamin B12, folic acid and iron deficiency:** ⟶ anemia (various types) – fatigue and weakness.
- **Vitamin D, calcium:** ⟶ muscle cramps - osteomalacia and osteoporosis.
- **Vitamin K and other coagulation factor:** ⟶ Bleeding tendencies.

REMEMBER:
Vit K: needed for synthesis of coagulation factor (factor 2, 5, 7, 9).
Vit C: needed for proper synthesis of collagen fibers (deficiency ⟶ bruising).

Diagnosis

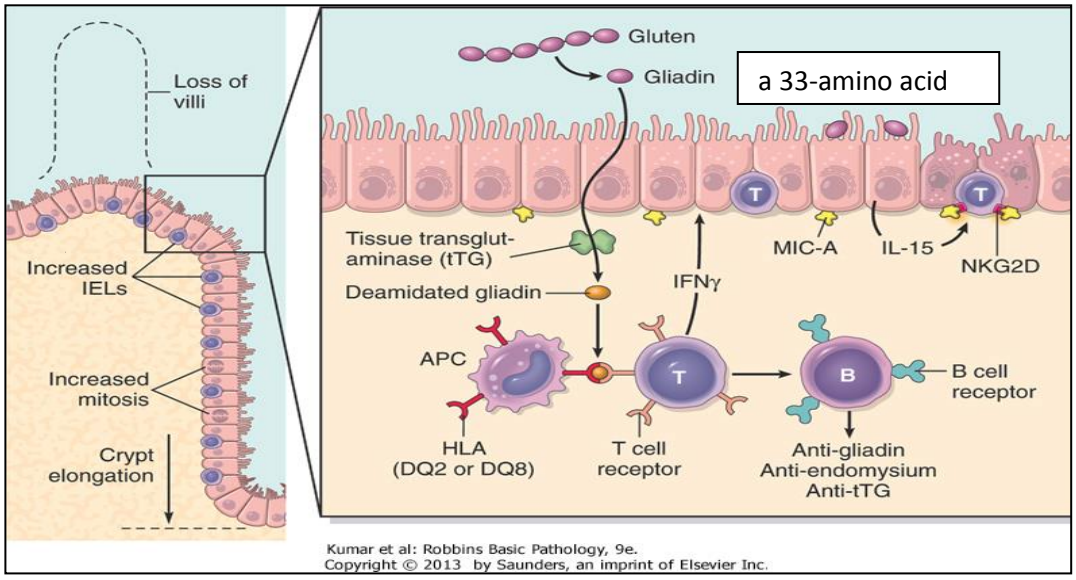
There is no specific test for malabsorption diagnosis. Investigation is guided by symptoms and signs:

1- Fecal fat study to diagnose steatorrhea.
2- Blood tests.
3- Stool studies.
4- **Endoscopy** (Biopsy of small bowel). Is really helpful in diagnosis of small bowel diseases like (celiac).

Celiac disease

- An immune reaction to Gliadin fraction of the wheat protein gluten in genetically predisposed persons more in European white.
- It is usually diagnosed in childhood – mid adult.
- Patients have raised antibodies to gluten autoantibodies.
- Highly specific association with **class II HLA DQ2** (haplotypes DR-17 or DR5/7) and, to a lesser extent, **DQ8** (haplotype DR-4).

Pathogenesis:



- Gluten is digested by luminal and brush boarder enzymes into amino acids and peptides, including a 33-amino acid gliadin peptide that is resistant to degradation by gastric, pancreatic, and small intestinal proteases.

- Gliadin is deamidated by tissue transglutaminase and is then able to interact with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells. This will lead to the activation of the T-cells that will produce cytokines (TNF-alpha, IFN-gamma) which will lead to "tissue damage" .

- The other mechanism is: Deamidated gliadin peptides induce epithelial cells to produce the cytokine IL-15, which in turn triggers activation and proliferation of CD8+ intraepithelial lymphocytes ⟶ (tissue damage) (both mechanisms occur together).

Note: One of the manifestations of celiac disease is high levels (infiltration) of CD8+ (T-lymphocytes) cells in the surface epithelium. So one of the histological methods of diagnosis is to count the number of T-lymphocytes, if T-lymphocytes > 30 per 100 cells ⟶ indicates early celiac disease.

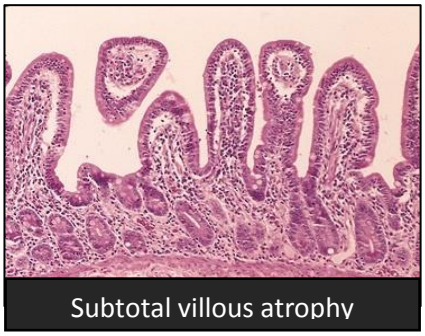
Clinical features: Typical presentation:

- GI symptoms that characteristically appear at age 9-24 months.
- Symptoms begin at various times after eating gluten-containing food.

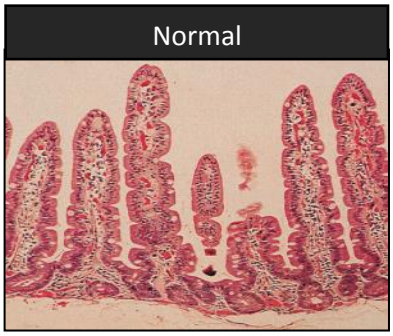
A relationship between the age of onset and the type of presentation;

- Infants and toddlers: GI symptoms and failure to thrive.
- Childhood: minor GI symptoms, inadequate rate of weight gain.
- Young adults: anemia is the most common form of presentation.
- Adults and elderly: GI symptoms are more prevalent. (Gasses, pain...).

Histology:


Subtotal villous atrophy

1- Mucosa is flattened with marked villous atrophy.
2- Increased intraepithelial lymphocytosis.
3- Crypt elongation.


Normal


Total villous atrophy

Diagnosis:

- Clinical documentations of malabsorption.
  Stool with ↑ Fat
- Serology is +ve for IgA to tissue transglutaminase or IgG to deamidated gliadin or anti-endomysial antibodies.
- Small intestine biopsy demonstrates villous atrophy.
- Improvement of symptom and mucosal histology on gluten withdrawal from diet → (wheat, barley, flour). (If we do a biopsy after 2-3 months of withdrawal we will see : villous → back to normal "regeneration")

Other grains, such as rice and corn flour, do not have such an effect.

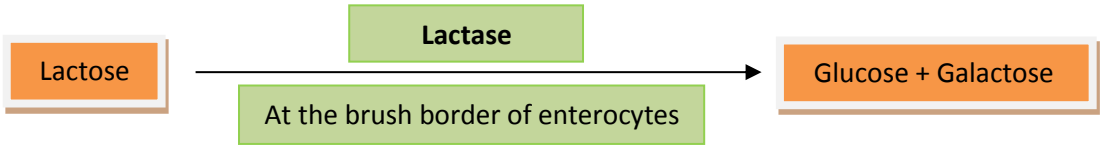
Complications:

- **Osteopenia, osteoporosis.**
- **Infertility in women.**
- **Short stature, delayed puberty, anemia.**
- **Malignancies,** [intestinal T-cell lymphoma]. Very rare in healthy normal people. Patients with celiac disease have 10 to 15% risk of developing GI lymphoma.
- **DDX Tropical sprue.** Is due to infection by bacteria, usually after visiting tropical areas (chronic diarrhea, weight loss …). Marked with abnormal flattening of the villi of the entire small intestine and inflammation of the lining, while in celiac disease it is usually the proximal part of the small intestine (duodenum and jejunum) that is going to have villi atrophy.

Lactose Intolerance

Pathophysiology:

Lactose is a type of sugar found in milk and other dairy products. Lactose intolerance develops when the small intestine does not make enough amount of an enzyme called "lactase". The body needs this enzyme to digest lactose.



Lactose intolerance: Low or absent activity of the enzyme lactase.

Causes: It's either inherited or acquired deficiency:

A) Inherited lactase deficiency:

1- Congenital lactase deficiency (extremly rare).

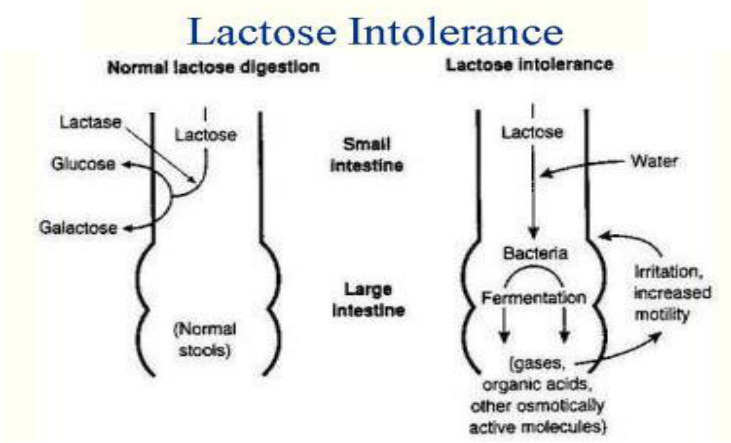
2- Childhood-onset and adult-onset lactase deficiency (common): Genetically programmed progressive loss of the activity of the small intestinal enzyme lactase.

B) Acquired lactase deficiency: (Transient)

Secondary lactase deficiency due to intestinal mucosal injury by an infectious, allergic, or inflammatory process.

Clinical Features:

- Bloating.
- Abdominal discomfort.
- Flatulence → 1 hour to a few hours after ingestion of milk products.



Diagnosis:

- Empirical treatment with a lactose-free diet, which results in resolution of symptoms; (A 3-week trial of a diet that is free of milk and milk products is a satisfactory trial to diagnose lactose intolerance).
- Hydrogen breath test (Most accurate).

Hydrogen breath test:

- An oral dose of lactose is administered.
- The sole source of H_2 is bacterial fermentation (by normal flora).
- Unabsorbed lactose makes its way to colonic bacteria, resulting in excess breath H_2.
- Increased exhaled H_2 (+) after lactose ingestion suggests lactose malabsorption.

Note: due to bacterial fermentation gasses are produced, and one of these gasses is hydrogen.
Absorbed by the intestines → respiratory tract → exhaled out of the body.
Normally, hydrogen is not found in our body.

Summary (from Robbins Basic Pathology)

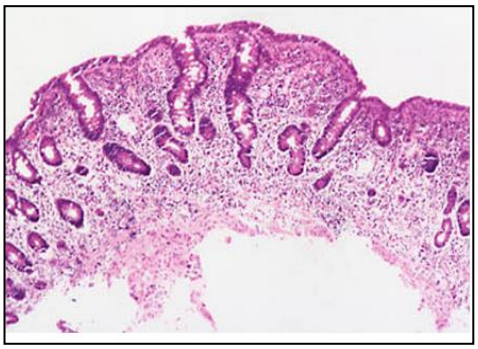
Celiac disease is an immune-mediated enteropathy triggered by the ingestion of gluten-containing grains. The malabsortive diarrhea in celiac disease is due to loss of brush boarder surface area and, possibly, deficient enterocyte maturation as a result of immune-mediated epithelial damage.

Lactase deficiency causes an osmotic diarrhea owing to the inability to break down or absorb lactose.

Questions

1- What effect does this process have on the surface area available for absorption?

Flattening of the villi greatly decreases the surface area available for absorption.



2- Exposure to what dietary antigen is thought to be the cause of these changes?

Gluten (specifically, the gliaden constituent of this protein)

3- Will these histologic changes resolve with dietary modification?

Yes

4- A 16-year-old girl complains of chronic abdominal distention, flatulence, and diarrhea after drinking milk. Elimination of milk and other dairy products from the patient's diet relieves these symptoms. This example of malabsorption is caused by a functional deficiency of which of the following enzymes associated with the intestinal brush border membrane?

(A) Disaccharidase.
(B) Glycogenphosphorylase.
(C) Hyaluronidase.
(D) Mannosidase.
(E) Sphingomyelinase.

5- A 4-year-old girl is brought to the physician because her parents noticed that she has been having pale, fatty, foul-smelling stools. The patient is at the 50th percentile for height and 10th percentile for weight. Her symptoms respond dramatically to a gluten-free diet. Which of the following is the most likely diagnosis?

(A) Celiacsprue
(B) Cystic fibrosis of the
(C) Ménétrierdisease
(D) Tropicalsprue
(E) Whippledisease

Answers:

- 4- A
- 5- A

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليَ عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us: 432PathologyTeam@gmail.com